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FILE 'CAPLUS' ENTERED AT 09:48:01 ON 11 FEB 2003

=> S ((CATALYTIC OR CATALYZES OR CATALYTIC OR CATALYZED)(5A)ANTIBOD?) OR ABZYME
        338979 CATALYTIC
            26 CATALYTICS
        338988 CATALYTIC
                  (CATALYTIC OR CATALYTICS)
         28953 CATALYZES
        338979 CATALYTIC
            26 CATALYTICS
        338988 CATALYTIC
                  (CATALYTIC OR CATALYTICS)
        198717 CATALYZED
             1 CATALYZEDS
        198717 CATALYZED
                  (CATALYZED OR CATALYZEDS)
        367189 ANTIBOD?
          1915 (CATALYTIC OR CATALYZES OR CATALYTIC OR CATALYZED)(5A)ANTIBOD?
           217 ABZYME
           133 ABZYMES
           257 ABZYME
                  (ABZYME OR ABZYMES)
L1        1936 ((CATALYTIC OR CATALYZES OR CATALYTIC OR CATALYZED)(5A)ANTIBOD?)
                  OR ABZYME

=> S COVALENTLY REACTIVE ANTIGEN ANALOG;S CRAA;S MEDICAL;S DISEASE;S ELECTROPHILIC
         35207 COVALENTLY
        225001 REACTIVE
           126 REACTIVES
        225085 REACTIVE
                  (REACTIVE OR REACTIVES)
        230512 ANTIGEN
        183020 ANTIGENS
        285572 ANTIGEN
                  (ANTIGEN OR ANTIGENS)
        183858 ANALOG
        170549 ANALOGS
        297485 ANALOG
                  (ANALOG OR ANALOGS)
L2           3 COVALENTLY REACTIVE ANTIGEN ANALOG
                  (COVALENTLY(W)REACTIVE(W)ANTIGEN(W)ANALOG)


             7 CRAA
             1 CRAAS
L3           8 CRAA
                  (CRAA OR CRAAS)


          66240 MEDICAL
             26 MEDICALS
L4        66257 MEDICAL
                  (MEDICAL OR MEDICALS)


         578472 DISEASE
         158529 DISEASES
L5       656345 DISEASE
                  (DISEASE OR DISEASES)


          21572 ELECTROPHILIC
              5 ELECTROPHILICS
L6        21574 ELECTROPHILIC
                  (ELECTROPHILIC OR ELECTROPHILICS)

=> S L2,L3
L7           11 (L2 OR L3)

=> D 1-11 CBIB ABS
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L7 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2003 ACS
2002:787409 Document No. 137:368063 Prospects for immunotherapeutic proteolytic antibodies. Zhou, Yong-Xin; Karle, Sangeeta; Taguchi, Hiroaki; Planque, Stephanie; Nishiyama, Yasuhiro; Paul, Sudhir (Department of Pathology and Laboratory Medicine, Chemical Immunology and Therapeutics Research Center, Dep. Pathology and Lab. Medicine, University of Texas-Houston Medical School, Houston, TX, 77030, USA). Journal of Immunological Methods, 269(1-2), 257-268 (English) 2002. CODEN: JIMMBG. ISSN: 0022-1759. Publisher: Elsevier Science B.V..
AB A review. Monoclonal antibodies are suitable for therapeutic applications by virtue of their excellent target binding characteristics (specificity, affinity) and long half-life in vivo. Catalytic antibodies (CAbs) potentially represent a new generation of therapeutics with enhanced antigen inactivation capability. Here, the authors describe prospects for development of therapeutic CAbs to the envelope protein gp120 of HIV. The strategy consists of exploiting the natural tendency of the immune system to synthesize germline-encoded, serine protease-like CAbs. Lupus patients were found to develop antibodies to a conserved component of the CD4 binding site of gp120, potentially offering a means to obtain human antibodies expressing broad reactivity with various HIV strains. ***Covalently*** ***reactive*** ***antigen*** ***analogs*** (CRAs) capable of selective recognition of nucleophilic Abs were synthesized and applied to isolate Fv and L chain catalysts from lupus phage repertoires. CRA binding by the recombinant Ab fragments was statistically correlated with catalytic cleavage of model peptide substrates. A peptidyl CRA composed of residues 421-431 with a phosphonate diester moiety at its C terminus was validated as a reagent that combines noncovalent and covalent binding interactions in recognition of a gp120ase L chain. A general challenge in the field is the apparent instability of the catalytic conformation of the Abs. In ref. to therapy of HIV infection, assurance is required that the Abs recognize the native conformation of gp120 expressed as a trimer on the virus surface.

L7 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2003 ACS
2002:692705 Synthesis of a ***covalently*** ***reactive*** ***antigen*** ***analog*** derived from a conserved sequence of HIV-1 gp120. Taguchi, Hiroaki; Nishiyama, Yasuhiro; Burr, Gary S.; Karle, Sangeeta A.; Paul, Sudhir (Chemical Immunology Research Center, Department of Pathology and Laboratory Medicine, University of Texas-Houston Medical School, Houston, TX, 77030, USA). Peptides: The Wave of the Future, Proceedings of the Second International and the Seventeenth American Peptide Symposium, San Diego, CA, United States, June 9-14, 2001, 1033-1034. Editor(s): Lebl, Michal; Houghten, Richard A. American Peptide Society: San Diego, Calif. ISBN: 0-9715560-0-8 (English) 2001. CODEN: 69DBAL.
AB Unavailable

L7 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2003 ACS
2002:84857 Document No. 136:332685 Study on liquid alkali developing type solder resists: reaction between dibasic acid half-ester with epoxy compound. Zeng, Zhao-Hua; Yang, Jian-Wen; Qin, Hai-Ding; Chen, Yong-Lie (Institute of Polymer Science, School of Chemistry and Chemical Engineering, Zhongshan University, Canton, 510275, Peop. Rep. China). Yingyong Huaxue, 19(1), 18-21 (Chinese) 2002. CODEN: YIHUED. ISSN: 1000-0518. Publisher: Yingyong Huaxue Bianji Weiyuanhui.
AB Reaction of dibasic acid half-ester with epoxy compd. has been investigated as function of factors affecting the reaction between carboxyl groups and epoxy using half-esters of a series of acid: maleic acid(MAM), succinic acid(SAM), phthalic acid(PAM), cis-1,2,3,6-tetrahydrophthalic acid(H4PAM) and cis-hexahydrophthalic acid(H6PAM), and Ph glycidyl ether(PGE) as model compds. It was found that higher reactivity would be achieved for the dibasic acid half-esters with smaller mol. size or stronger acidity. In the case of reaction between maleic acid monomethyl eater(MAM) and PGE, the catalytic activity of the catalysts decreased in the order of chromium acetylacetonate ( ***CrAA*** )>tetramethyl ammonium bromide(TMAB)>1-methylimidazole(MI) >N,N-dimethyl benzylamine(DMBA). The effects of solvent polarity and temp. on the reaction has also been examd.

L7 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2003 ACS
2001:407286 Document No. 135:134458 Carbon-source-dependent transcriptional

control involved in the initiation of cellular differentiation in Streptomyces griseus. Ueda, Kenji; Endo, Kouki; Takano, Hideaki; Nishimoto, Madoka; Kido, Yasumasa; Tomaru, Yasuhiro; Matsuda, Kouichi; Beppu, Teruhiko (Department of Applied Biological Sciences, Nihon University, Fujisawa, 252-8510, Japan). Antonie van Leeuwenhoek, 78(3-4), 263-268 (English) 2000. CODEN: ALJMAO. ISSN: 0003-6072. Publisher: Kluwer Academic Publishers.

AB Carbon source is one of the environmental factors that affects cellular differentiation of Streptomyces. We have identified the ***craA*** gene as a putative neg. regulator involved in the carbon-source-dependent initiation of cellular differentiation in Streptomyces griseus. Carbon-source-dependent transcriptional repression of ***craA*** , which is caused by binding of a putative repressor protein to its promoter region, is proposed to result in the initiation of aerial mycelium formation. The presence of a ***craA*** homolog in the chromosome of Streptomyces coelicolor A3(2) implicates the existence of a similar regulatory mechanism in this organism. The repression of ***craA*** -promoter activity in glucose media could be alleviated not only by replacing glucose with maltose but also by supplying copper, which suggests that the stimulatory effect of copper on cellular differentiation in Streptomyces is exerted via abolishment of glucose-repression of ***craA*** .

L7 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2003 ACS

1999:648244 Document No. 132:31601 A putative regulatory element for carbon-source-dependent differentiation in Streptomyces griseus. Ueda, Kenji; Matsuda, Kouichi; Takano, Hideaki; Beppu, Teruhiko (Department of Applied Biological Sciences, Nihon University, Fujisawa, 252-8510, Japan). Microbiology (Reading, United Kingdom), 145(9), 2265-2271 (English) 1999. CODEN: MROBEO. ISSN: 1350-0872. Publisher: Society for General Microbiology.

AB To identify neg. regulatory genes for cellular differentiation in Streptomyces griseus, DNA fragments repressing the normal developmental processes were cloned on a high-copy-no. plasmid. One of these DNA fragments markedly repressed aerial mycelium and spore formation on solid media contg. glucose or galactose, but not on media contg. maltose or mannitol. The fragment contained three complete ORFs; precise subcloning revealed that a 249 bp fragment located in the promoter region between ORF1 and ORF3 was sufficient for repression. Quantification of the promoter activities by using a thermostable malate dehydrogenase gene as a reporter showed that the promoter for ORF3 (PORF3) maintained high activity in mycelia grown in the presence of glucose but lost activity rapidly in maltose medium. PORF3 activity increased markedly when the promoter sequence was introduced on a high-copy-no. plasmid. The results suggested that carbon-source-dependent deactivation of PORF3 mediated by a transcriptional repressor may initiate differentiation in S. griseus.

L7 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2003 ACS

1999:626226 Document No. 131:241986 Methods for identifying inducers and inhibitors of proteolytic antibodies, compositions and their uses. Paul, Sudhir; Gololobov, Gennady; Smith, Larry (University of Nebraska Board of Regents, USA). PCT Int. Appl. WO 9948925 A1 19990930, 158 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US6325 19990323. PRIORITY: US 1998-46373 19980323.

AB Disclosed herein are ***covalently*** ***reactive*** ***antigen*** ***analogs*** comprising epitope of tumor necrosis factor, EGF receptor, interleukin 1, gp120, gp160, gag, pol, hepatitis B surface antigen, bacterial exotoxin, EGF, TGF.alpha., p53, prostate-specific antigen, carcinoembryonic antigen, prolactin, human chorionic gonadotropin, c-myc, c-fos, c-jun, HER-2, prolactin receptor, steroid receptor or interleukin 4.. The antigens of the invention may be used to stimulate prodn. of catalytic antibodies specific for predetd. antigens assocd. with particular medical disorders. The antigen analogs may also be used to permanently inactivate endogenously produced catalytic antibodies produced in certain autoimmune diseases as well as in certain

lymphoproliferative disorders. The invention also provides methods for identifying, isolating and prodn. of catalytic antibodies with therapeutic value.

L7 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2003 ACS
1992:445475 Document No. 117:45475 Brefeldin A-resistant mutants of human epidermoid carcinoma cell line with structural changes of the Golgi apparatus. Seguchi, Tadashi; Goto, Yukiko; Ono, Mayumi; Fujiwara, Toshiyuki; Shimada, Tatsuo; Kung, Hsiangfu; Nishioka, Mikio; Ikehara, Yukio; Kuwano, Michihiko (Dep. Biochem., Oita Med. Univ., Oita, 879-55, Japan). Journal of Biological Chemistry, 267(16), 11626-30 (English) 1992. CODEN: JBCHA3. ISSN: 0021-9258.
AB Brefeldin A (BFA)-resistant cell lines, KB/BF-1 and KB/BF-2, were isolated from the human epidermoid carcinoma KB cell line. The BFA-resistant phenotypes have been stably maintained for more than 3 mo in the absence of BFA. KB/BF-1 and KB/BF-2 showed 10-30-fold higher resistance to cytotoxicity of BFA but were 2-3-fold more sensitive to monensin and nigericin, than KB cells. KB/BF-1 showed aberrant structures of the Golgi complex with poorly developed cisternae surrounded by many small vesicles. Immunocytochem. studies were done with antibodies against a Golgi-specific antigen (chronic rheumatoid arthritis antigen) and a coatomer subunit (.beta.-subunit for coat proteins of non-clathrin-coated vesicles). Golgi-specific markers were distributed into the small vesicles which were localized diffusely in cytoplasm of KB/BF-1 cells. Such Golgi markers were obsd. in a strictly confined perinuclear region of the parental KB cells, whereas in the mutant cells the markers were distributed more diffusely in dot-like structures at perinuclear regions. In addn., when exposed to BFA, the mutant and parental cells showed a different distribution of these markers. Synthesis and maturation of low-d. lipoprotein receptor showed apparently slower rates in processing of low d. lipoprotein receptor in KB/BF-1 and KB/BF-2 cells than those obsd. in their parental KB cells. Protein secretion in KB/BF-1 and KB/BF-2 cells was .apprx.30% less than that in KB cells. Much less inhibition by BFA on the secretion was obsd. in KB/BF-1 and KB/BF-2 cells. A BFA-resistant mutation in BFA-resistant KB cell lines appears to affect assembly of the Golgi app. as well as some Golgi-specific functions.

L7 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2003 ACS
1990:90498 Document No. 112:90498 Critical reflection activation analysis - a new near-surface probe. Gunn, J. M. F.; Trohidou, K. N. (Rutherford Appleton Lab., Chilton/Didcot/Oxon., OX11 0QX, UK). Journal of Physics D: Applied Physics, 22(7), 1001-3 (English) 1989. CODEN: JPAPBE. ISSN: 0022-3727.
AB A new surface anal. technique, crit. reflection activation anal. ( ***CRAA*** ) is proposed with neutrons. This technique allows accurate depth profiling of impurities .ltoreq.100 .ANG. beneath a surface. The depth profile of the impurity is simply related to the induced activity as a function of the angle of reflection. The technique is practical, its accuracy is estd.

L7 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2003 ACS
1989:65414 Document No. 110:65414 Critical reflection activation analysis - a new near-surface probe. Gunn, J. M. F.; Trohidou, K. N. (Rutherford Appleton Lab., Didcot/Oxon., OX11 0QX, UK). Rutherford Appleton Lab., [Rep.] RAL, RAL-88-072, 7 pp. (English) 1988. CODEN: RALRDQ.
AB A new surface anal. technique, Crit. Reflection Activation Anal. ( ***CRAA*** ) is proposed. This technique allows accurate depth profiling of impurities .ltoreq. 100 .ANG. beneath a surface. The depth profile of the impurity is simply related to the induced activity as a function of the angle of reflection. The technique is practical, and its accuracy is estd. With available n sources, detection of a wide range of elements is possible.

L7 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2003 ACS
1980:491406 Document No. 93:91406 Sol particle immunoassay (SPIA). Leuvering, J. H. W.; Thal, P. J. H. M.; Van der Waart, M.; Schuurs, A. H. W. M. (Organon Sci. Dev. Group, Oss, 5340 BH, Neth.). Journal of Immunoassay, 1(1), 77-91 (English) 1980. CODEN: JOUIDK. ISSN: 0197-1522.
AB Inorg. (metal) colloidal particles were used as a label for immunoassays. Dose-response curves for human placental lactogen (HPL) and human chorionic gonadotropin (HCG) were obtained with sandwich immunoassays by

using conjugates consisting of antibody-coated colloidal Au or Ag particles. Several techniques were used to measure the amt. of bound conjugate: colorimetry and C-rod at. absorption spectrometry ( ***CRAAS*** ). At higher antigen concns., the results of the assay could be read by the naked eye. By using Au particles as the label and ***CRAAS*** , the detection limit for a sandwich HPL SPIA of 1.4 pmol/L was equal to that of an optimized competitive radioimmunoassay. When using a colorimeter, the detection limit for HPL of this SPIA was 5.4 pmol/L, which was superior to that of a corresponding sandwich enzyme immunoassay. HPL and HCG were also simultaneously detd., using microtitrn. plates, coated with a mixt. of anti-HPL and anti-HCG, and a mixt. of Ag particle anti-HPL conjugate and Au particle anti-HCG conjugate. ***CRAAS*** was used to measure the bound Ag and Au conjugate. This simultaneous assay requires more work to obtain better sensitivities.

L7 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2003 ACS
1980:132212 Document No. 92:132212 Sedimental aspects of the phosphate concentration in the Bu- ***Craa*** (western Sahara) deposit. Canto Romera, J. M. (Spain). Tecniterrae, 4(24), 14-30 (Spanish) 1978. CODEN: TECNDJ. ISSN: 0378-4819.
AB The phosphate deposits of Bu- ***Craa*** consist of apatite [64476-38-6] 92, sand 3, calcite [13397-26-7] 2, clay 2, hematite 0.5, and others (domomite, fluorite, feldspar, etc.) 1.5%. Anal. indicates the presence of 75% Ca phosphate. The formation theories proposed by A.V. Kazakow (1937) and by M. Slansky (1964) are confirmed, indicating the phosphate is a secondary mineral transported from elsewhere.

=> S L4 AND L1;S L5(6A)L1;S L6 AND L1
L8 17 L4 AND L1

L9 32 L5(6A)L1

L10 13 L6 AND L1

=> S L8,L9,L10
L11 58 (L8 OR L9 OR L10)

=> S L11 NOT L7
L12 57 L11 NOT L7

=> D 1,3-9,11-13,16,22,24-26,33,35,36,39-42,46,49 CBIB ABS

L12 ANSWER 1 OF 57 CAPLUS COPYRIGHT 2003 ACS
2002:832912 Document No. 137:351494 Method for producing catalytic antibodies, antigens for immunization and nucleotide sequences. Gabibov, Alexandr Gabibovich; Kolesnikov, Alexandr Vladimirovich; Ponomarenko, Natalya Alexandrovna; Alexandrovna, Elena Sergeevna; Borobiev, Ivan Ivanovich; Demin, Alexandr Viktorovich (ASGL- Farmatsevticheskie Innovatsii, Zakrytoe Aktsionernoe Obschestvo, Russia). PCT Int. Appl. WO 2002086058 A2 20021031, 46 pp. DESIGNATED STATES: W: AU, BG, BY, CA, CN, CZ, EE, HU, IL, JP, KR, NO, PL, SK, UA, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR. (Russian). CODEN: PIXXD2. APPLICATION: WO 2002-RU177 20020418. PRIORITY: RU 2001-110759 20010424.
AB The aim of the invention is to develop a method for producing catalytic antibodies to proteins and peptides, in particular to gp120, using animals with spontaneous or induced autoimmune pathologies. Various methods for producing catalytic antibodies are disclosed. The inventive methods make it possible to create a catalytic vaccine which, when injected to a patient exhibits adhesive properties in relation to specific antigen simultaneously with antigen-degrading function, thereby inhibiting the progression of the disease. Said invention discloses the method for the autoimmunization of SJL mice by fusion proteins contg. a classical peptide epitope (for example, myelin basic protein or fragments thereof) and the potential substrate of the target catalytic antibody (for example, HIV-1 gp120 or fragments thereof). The invention also comprises the method for immunizing autoimmune animals with highly reactive chem. compds., which

can select catalytic clones contg. peptide fragments of proteolytically degraded gp120.

L12 ANSWER 3 OF 57 CAPLUS COPYRIGHT 2003 ACS
2002:787402 Document No. 138:51716 Human ***catalytic*** RNA- and DNA-hydrolyzing ***antibodies*** . Nevinsky, Georgy A.; Buneva, Valentina N. (Novosibirsk Institute of Bioorganic Chemistry, Siberian Division of Russian Academy of Sciences, Novosibirsk, 630090, Russia). Journal of Immunological Methods, 269(1-2), 235-249 (English) 2002. CODEN: JIMMBG. ISSN: 0022-1759. Publisher: Elsevier Science B.V..
AB A review. In patients with autoimmune diseases, anti-idiotypic antibodies directed to nucleoprotein complexes, DNA, and enzymes that participate in nucleic acid metab. may be induced spontaneously by primary antigens and can have characteristics of the primary antigen, including catalytic activity. The first natural ***catalytic*** ***antibody*** , now termed ***abzyme*** , which hydrolyzes intestinal vasoactive peptide, was discovered by Paul et al. [Science 244 (1989) 1158]. Subsequently, other ***abzymes*** able to hydrolyze proteins, DNA, RNA, or polysaccharides have been found in the sera of patients with autoimmune and also viral pathologies. Further, we have discovered in the milk of healthy human mothers antibodies that catalyze the hydrolysis of RNA, DNA, nucleotides, and the phosphorylation of lipids and proteins. The phenomenon of catalysis by autoantibodies is extremely interesting and can potentially be applied to many different objectives including new types of efficient catalysts, evaluation of the functional roles of ***abzymes*** in innate and adaptive immunity, and understanding of certain aspects of self-tolerance and of the destructive responses in autoimmune diseases. In this review, we collate methods for purifying and characterizing natural ***abzymes*** esp. those catalyzing DNA and RNA hydrolysis. We also describe new methods that we have developed to provide rigorous criteria that catalytic activity is an intrinsic property of some antibodies. Some major current themes are discussed as well as potential applications of ***abzymes*** in scientific, ***medical*** , and biotechnol. fields.

L12 ANSWER 4 OF 57 CAPLUS COPYRIGHT 2003 ACS
2002:787400 Document No. 137:368062 Evolution of catalytic antibody repertoire in autoimmune mice. Nishi, Yoshisuke (Laboratory of Life Science and Biomolecular Engineering, Japan Tobacco, Inc., Kanagawa, Yokohama, 227-8512, Japan). Journal of Immunological Methods, 269(1-2), 213-233 (English) 2002. CODEN: JIMMBG. ISSN: 0022-1759. Publisher: Elsevier Science B.V..
AB A review. The authors' effort has been devoted to exploring the immunol. evolution of catalytic antibodies (catAbs) in MRL/lpr mice. Using different phosphonate haptens, they confirmed that catAbs could be recovered at higher incidence from one of the autoimmune mouse strains (MRL/lpr) than from a conventional mouse strain (BALB/c). The authors then tried to elucidate the evolution of catAbs in the autoimmune repertoire based on sequence anal. Here, they emphasize that catAbs were uniquely obtained from a subset of the repertoire of an autoimmune mouse strain, but they were not obtained from the repertoire of a normal mouse strain.

L12 ANSWER 5 OF 57 CAPLUS COPYRIGHT 2003 ACS
2002:787398 Document No. 138:51781 ***Catalytic*** ***antibodies*** in clinical and experimental pathology: human and mouse models. Ponomarenko, Natalya A.; Durova, Oxana M.; Vorobiev, Ivan I.; Aleksandrova, Elena S.; Telegin, Georgy B.; Chamborant, Olga G.; Sidorik, Lyudmila L.; Suchkov, Sergei V.; Alekberova, Zemfira S.; Gnuchev, Nikolay V.; Gabibov, Alexander G. (Shemyakin and Ovchinnikov Institute of Bioorganic Chemistry, Moscow, V-437, Russia). Journal of Immunological Methods, 269(1-2), 197-211 (English) 2002. CODEN: JIMMBG. ISSN: 0022-1759. Publisher: Elsevier Science B.V..
AB Most of the data accumulated through studies on natural catalytic autoantibodies indicate that prodn. scales up markedly in pathol. abnormalities. We have previously described an increased level of DNA-hydrolyzing autoantibodies in the sera of patients with various autoimmune disorders [systemic lupus erythematosus (SLE), rheumatoid arthritis, scleroderma], HIV infection and lymphoproliferative diseases accompanied by autoimmune manifestations. In the present study, we show that an increased level of catalytic activity of autoantibodies can be

obsd. in the sera of autoimmune mice, thus providing a fundamental insight into the ***medical*** relevance of ***abzymes*** . Polyclonal autoantibodies purified from sera of NZB/W, MRL-lpr/lpr and SJL/J mice show proteolytic and DNA-hydrolyzing activities, as opposed to those harvested from non-autoimmune BALB/c mice. The expressiveness of the catalytic activity was strongly dependent on the age of the animal. The highest levels of catalytic activity were found in the sera of mice aged between 8 and 12 mo; the lowest level was typical of younger animals whose age ranged from 6 to 8 wk. Specific inhibition assays of the catalytic activities were performed to throw light on the nature of the ***abzyme*** activity. Within a cohort of aging animals, a strong correlation between marked autoimmune abnormalities and levels of catalytic activities has been established. Nonimmunized SJL/J mice revealed specific immune responses to myelin basic protein (MBP), skeletal muscle myosin (skMyo) and cardiac myosin (Myo), and highly purified antibodies from their serum show specific proteolytic attack against the target antigens. This finding prompted us to undertake a more detailed study of specific antibody-mediated proteolysis in diseased humans. A targeted catalytic response was originally demonstrated against MBP and Myo in multiple sclerosis and myocarditis patients, resp.

L12 ANSWER 6 OF 57 CAPLUS COPYRIGHT 2003 ACS

2002:777955 Document No. 137:290932 Covalently reactive transition state analogs for use in therapeutic inhibition or production of ***catalytic*** ***antibodies*** . Paul, Sudhir; Nishiyama, Yasuhiro (Board of Regents, the University of Texas System, USA). PCT Int. Appl. WO 2002079223 A2 20021010, 87 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US10116 20020401. PRIORITY: US 2001-PV280624 20010331.

AB Covalently reactive transition state analogs (CRTSAs) R1-E-R2 (R1 = peptide epitope of target antigen; E = ***electrophilic*** , covalently reactive, charged center; R2 = electron donating or withdrawing group optionally attached to another peptide) and their use in inhibiting ***disease*** -related ***catalytic*** ***antibodies*** or in stimulating prodn. of ***catalytic*** ***antibodies*** with desirable activities are disclosed. The CRTSAs may also be used to select phage display ***catalytic*** ***antibodies*** or to select B cells displaying ***catalytic*** ***antibodies*** on their surface. Thus, N-acyl derivs. of amino(4-amidinophenyl)methanephosphonate esters were prepd. These phosphonates irreversibly inhibited trypsin, thrombin, and ***catalytic*** ***antibodies*** . Other phosphonates were used to isolate catalytically active subtilisin mutants or proteolytically active Fv and L chains from phage libraries.

L12 ANSWER 7 OF 57 CAPLUS COPYRIGHT 2003 ACS

2002:522784 Document No. 137:92723 Method for determining catalytic antibodies and their use in the diagnosis of systemic autoimmune diseases. Suchkov, S. V.; Gabibov, A. G.; Ievleva, E. S.; Ivanenko, T. V.; Alekberova, Z. S.; Shuster, A. M. (Moskovskii Oblastnoi Nauchno-Issledovatel'skii Klinicheskii Institut, Russia). Russ. RU 2173464 C1 20010910, No pp. given (Russian). CODEN: RUXXE7. APPLICATION: RU 2000-107061 20000323.

AB The invention involves selecting the IgG antibody fraction from blood, adding the substrate, and incubating the produced reaction mixt. followed with gel electrophoresis. Plasmid DNA is used as the substrate taken in 1 .mu.g : 2-10 .mu.g proportion with the IgG antibody fraction. The reaction mixt. is incubated for 25-30 min at 35-37 C.degree.. The electrophoresis is carried out in 0.8% agar gel under 15 mA d.c. for 20-30 min. The degree of straightening of plasmid DNA is interpreted in terms of the catalytic antibodies presence. The disease diagnosis involves clin. lab. studies and the electrophoretic anal. of sepd. catalytic autoantibodies. The diagnosis is set by the percentage of straightened plasmid DNA present. The linear form of plasmid DNA being detected in the amt. of .ltoreq.25% indicates the absence of the autoimmune process. The

amt. of linear DNA between 25-50% indicates a low degree of the autoimmune process activity. The value greater than 50% indicates a high degree of autoimmune activity. The method of linear dichroism can be used to det. catalytic autoantibodies when the autoimmune activity is high.

L12 ANSWER 8 OF 57 CAPLUS COPYRIGHT 2003 ACS
2002:507409 Document No. 137:293361 The distribution of DNA-abzymes in patients with different types of systemic and organ-specific autoimmune disorders. Suchkov, Sergei V.; Gabibov, Alexander G.; Gnuchev, Nikolai V.; Alekberova, Zemphira S. (MONIKI, M. M. Shemyakin & Yu. A. Ovchinnikov Institute of Bioorganic Chemistry, Russian Academy of Sciences, Moscow, Russia). Russian Journal of Immunology, 6(3), 309-312 (English) 2001. CODEN: RJIUAC. ISSN: 1028-7221. Publisher: Russian Society of Immunology.
AB The distribution of the DNA-abzymes in various kinds of systemic and organ-specific autoimmune states was studied by introducing a rapid and efficient assay procedure for screening large amts. of sera for the presence of DNA-abzymes. The study included 120 samples from patients with systemic lupus erythematosus (SLE), 82 with systemic scleroderma (SS), 72 with rheumatoid arthritis (RA), 88 with localized scleroderma (LS), 60 with discoid lupus erythematosus (DLE) and 198 with autoimmune uveitis (AU). The largest cohort of patients tested and possessing DNA-abzymes of IgG class was a group of SLE. Sera of the rest of the patients showed seropositivity for DNA abzymes. Comparative anal. of levels of DNA-hydrolyzing activities among patients with SLE and RA showed that SLE is featured with the highest levels of DNA-hydrolyzing activity ranged from 12 to 1850 units as compared to 8-120 units in RA and 0.012-0.200 units in healthy individuals.

L12 ANSWER 9 OF 57 CAPLUS COPYRIGHT 2003 ACS
2002:332361 Document No. 136:321704 Methods and compositions for modifying biologically active target molecules with catalytic antibodies. Martin, Mark T. (Igen International, Inc., USA). PCT Int. Appl. WO 2002034933 A2 20020502, 61 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US31663 20011010. PRIORITY: US 2000-PV242125 20001020.
AB The invention concerns a method of modifying a target substance by contacting the target substance with a catalyst that catalyzes the modification of the target substance. In a preferred embodiment, the method comprises labeling a target substance by contacting the target substance with a label and a catalyst that catalyzes the attachment of the label to the target substance. Preferably, the catalyst catalyzes selectively the reaction between a specific target mol. and a specific label. The attachment of labels may be used to inactivate a biol. active target substance or otherwise modulate its activity. Alternatively, the method may be used to label the target mol. with a detectable label suitable for the sensitive detection of the target substance.

L12 ANSWER 11 OF 57 CAPLUS COPYRIGHT 2003 ACS
2002:37261 Document No. 137:107695 Recent advances of ***catalytic*** ***antibodies*** (2). Fujii, Ikuo; Tsumuraya, Takeshi (Research Institute for Bio-Molecular and Engineering, Japan). Fain Kemikaru, 30(22), 12-20 (Japanese) 2001. CODEN: FNKMAU. ISSN: 0913-6150. Publisher: Shi Emu Shi.
AB A review on application of antibodies as catalysts to chem. and ***medical*** studies.

L12 ANSWER 12 OF 57 CAPLUS COPYRIGHT 2003 ACS
2002:6117 Document No. 137:136706 Recent advances in ***catalytic*** ***antibodies*** . Fujii, Ikuo; Tsumuraya, Takeshi (Bio-Molecular Engineering Research Institute, Japan). Fain Kemikaru, 30(21), 5-15 (Japanese) 2001. CODEN: FNKMAU. ISSN: 0913-6150. Publisher: Shi Emu Shi.
AB A review on ***catalytic*** ***antibodies*** discussing induction

of ***catalytic*** ***antibodies*** and its applications to org. synthetic chem. and ***medical*** science.

L12 ANSWER 13 OF 57 CAPLUS COPYRIGHT 2003 ACS
2001:821499 Document No. 136:339263 A phenomenon of DNA-abzyme cross-reactivity and its significance for the mechanisms of cytotoxicity and apoptosis. Suchkov, S. V.; Gabibov, A. G.; Gnuchev, N. V. (MONIKI, Moscow, 129110, Russia). Russian Journal of Developmental Biology (Translation of Ontogenez), 32(5), 287-291 (English) 2001. CODEN: RJDBE2. ISSN: 1062-3604. Publisher: MAIK Nauka/Interperiodica Publishing.
AB The physiol. role of DNA-abzymes and their involvement in pathogenesis of different autoimmune disorders is still unknown. At the same time, a variety of properties and features of DNA-hydrolyzing autoantibodies have been studied. Here, the phenomenon of the cross-reactivity of DNA-abzymes with the nuclear matrix proteins was studied. The possible value of the phenomenon for the cytotoxic activity of DNA-hydrolyzing autoantibodies was debated as well. A new hypothesis is put forward regarding the DNA-abzymes formation based on the phenomenon of the cross-reactivity of polyclonal DNA-abzymes with nuclear matrix proteins free of native DNA. Preliminary results suggest that there are mechanisms of cytotoxicity mediated by DNA-abzymes and independent from the system of complement and cytotoxic T-lymphocytes.

L12 ANSWER 16 OF 57 CAPLUS COPYRIGHT 2003 ACS
2001:288037 Document No. 135:328577 Catalytically active antibodies and their possible biological function. Nevinskii, G. A.; Kanyshkova, T. G.; Semenov, D. V.; Buneva, V. N. (Novosibirsk. Inst. Bioorg. Khim., SO RAN, Novosibirsk, Russia). Vestnik Rossiiskoi Akademii Meditsinskikh Nauk (2), 38-45 (Russian) 2001. CODEN: VAMEE3. ISSN: 0869-6047. Publisher: Meditsina.
AB A review with refs. Investigations of recent decades lead to discovery of a new function of Igs: their ability to catalyze a large no. of various chem. processes, i.e. function as enzymes. Generation of and action catalytic antibodies obtained by immunization of animals by stable intermediates of chem. reactions are described in the review, as well as catalytic antibodies which appear in the blood of patients with various autoimmune disorders or virus-caused diseases and in the blood of healthy women at childbirth.

L12 ANSWER 22 OF 57 CAPLUS COPYRIGHT 2003 ACS
2000:517639 Document No. 133:331195 ***Catalytic*** ***antibodies*** . Blackburn, George Michael; Garcon, Arnaud (Department of Chemistry, The University of Sheffield, Sheffield, S3 7HF, UK). Biotechnology (2nd Edition), Volume 8b, 403-490. Editor(s): Kelly, D. R. Wiley-VCH Verlag GmbH: Weinheim, Germany. (English) 2000. CODEN: 58AHA6.
AB A review with .apprx.275 refs. refs. The topics discussed include approaches to hapten design, spontaneous features of ***antibody*** catalysis, how good are ***catalytic*** ***antibodies*** , changing the regio- and stereochem. of reactions, difficult processes (resoln. of diastereomers, cleavage of acetals and glycosides, phosphate ester cleavage, amide hydrolysis), reactive immunization, potential ***medical*** applications, and the industrial future of ***abzymes*** .

L12 ANSWER 24 OF 57 CAPLUS COPYRIGHT 2003 ACS
2000:214064 Document No. 133:13524 Design and synthesis of an .alpha.,.alpha.-difluorophosphinate hapten for ***antibody*** - ***catalyzed*** hydrolysis of organophosphorus nerve agents. Vayron, Philippe; Renard, Pierre-Yves; Valleix, Alain; Mioskowski, Charles (CEA, Service des Molecules Marquees, CE-Saclay, Gif sur Yvette, F-91191, Fr.). Chemistry--A European Journal, 6(6), 1050-1063 (English) 2000. CODEN: CEUJED. ISSN: 0947-6539. Publisher: Wiley-VCH Verlag GmbH.
AB In a new approach to the safe neutralization of organophosphorus chem. weapons, we designed a hapten to elicit ***catalytic*** ***antibodies*** with phosphatase activity. Here we report the synthesis of this .alpha.,.alpha.-difluorophosphinate hapten 6. Various methods for the introduction of the key .alpha.,.alpha.-difluoromethyl feature into the phosphinate hapten are discussed. The best results were obtained with the ***electrophilic*** gem-difluorinating agent N-fluorobenzenesulfonimide.

L12 ANSWER 25 OF 57 CAPLUS COPYRIGHT 2003 ACS
1999:285556 Document No. 131:126999 ***Catalytic*** ***antibodies*** . Blackburn, G. Michael; Datta, Anita; Denham, Hazel; Wentworth, Paul, Jr. (Krebs Institute, Department of Chemistry, University of Sheffield, UK). Advances in Physical Organic Chemistry, 31, 249-392 (English) 1998. CODEN: APORAO. ISSN: 0065-3160. Publisher: Academic Press.
AB A review with .apprx.240 refs. The topics discussed include a glossary, approaches to hapten design, spontaneous features of ***antibody*** catalysis, performance anal. of ***catalytic*** ***antibodies*** , a case study of an antibody anilidase, rescheduling regio- and stereo-chem. of chem. reactions, reactive immunization, ***medical*** potential of ***abzymes*** , and industrial potential of ***abzymes*** . (c) 1998 Academic Press.

L12 ANSWER 26 OF 57 CAPLUS COPYRIGHT 2003 ACS
1999:243683 Document No. 131:55559 Mechanism and functional role of antibody catalysis. Paul, Sudhir (Department of Pathology and Laboratory Medicine, University of Texas Medical School, Houston, TX, 77030, USA). Applied Biochemistry and Biotechnology, 75(1), 13-24 (English) 1998. CODEN: ABIBDL. ISSN: 0273-2289. Publisher: Humana Press Inc..
AB A review with 56 refs. The light (L) chain of a model antibody (Ab) was deduced to contain a serine protease-like catalytic site capable of cleaving peptide bonds. The catalytic site is encoded by a germline VL gene. The catalytic activity can potentially be improved by somatic sequence diversification and pairing of the L chain with the appropriate heavy chain. Autoimmune disease is assocd. with increased synthesis of antigen (Ag)-specific Abs, but the reasons for this phenomenon are not known. Only recently has attention turned to the functional role of the catalytic function. Preliminary studies confirm that the catalytic cleavage of peptide bonds is a more potent means to achieve Ag neutralization, compared to reversible Ag binding. Administration of a monoclonal Ab to VIP in exptl. animals induces an inflammatory response in the airways, suggesting that catalytic autoantibodies to this peptide found in airway disease and lupus are capable of causing airway dysfunction. The phenomenon of autoantibody catalysis can potentially be applied to isolate efficient catalysts directed against tumor or microbial Ags by exposing the autoimmune repertoire to such Ags or their analogs capable of recruiting the germline VL gene encoding the catalytic site.

L12 ANSWER 33 OF 57 CAPLUS COPYRIGHT 2003 ACS
1997:477916 Document No. 127:216815 Characterization of thyroglobulin-directed and polyreactive ***catalytic*** ***antibodies*** in autoimmune ***disease*** . Paul, Sudhir; Li, Lan; Kalaga, Ravishankar; O'Dell, James; Dannenbring, Robert E., Jr.; Swindells, Susan; Hinrichs, Steven; Caturegli, Patrizio; Rose, Noel R. (Departments Anesthesiology, Pathology and Microbiol., and Internal Medicine, Eppley Cancer Research Institute, Univ. Nebraska Medical Center, Omaha, NE, 68198, USA). Journal of Immunology, 159(3), 1530-1536 (English) 1997. CODEN: JOIMA3. ISSN: 0022-1767. Publisher: American Association of Immunologists.
AB Polyreactive and thyroglobulin (Tg)-directed proteolytic activities present in the serum IgG of healthy controls and patients with autoimmune disease were studied by electrophoretic sepn. of 125I-labeled Tg reaction products and spectrofluorometric measurement of Pro-Phe-Arg-methylcoumarinamide cleavage at the Arg-methylcoumarinamide bond. A decrease of the polyreactive proteolytic activity accompanying an increase of the Tg-cleaving activity in IgG from autoimmune thyroiditis (ATh) and systemic lupus erythematosus (SLE) was evident. The Tg, a known target of autoimmune reactions in ATh, was cleaved at lower levels by Abs from patients with this disease than from SLE patients. The Tg-cleaving and Tg-binding activities of the autoantibody prepns. were not correlated. Enhanced rates of cleavage at satg. substrate concns. (Vmax), not increased Tg-binding affinities, were evident in IgG prepns. with the greatest Tg-cleaving activity. Similarly, diminution of the polyreactive proteolytic activity in IgG from the autoimmune disease patients was due to decreased Vmax values, not decreased substrate-binding affinities. No cleavage of Tg by IgG from subjects with HIV-1 infection, or from mice hyperimmunized with an albumin-hapten conjugate was evident, suggesting that generation of Tg-cleaving Abs does not accompany V region affinity maturation in response to unrelated Ags. These observations establish Tg as a target of catalytic autoantibodies in SLE and ATh, suggest a transition from polyreactive proteolytic activity to autoantigen-directed

activity in autoimmune disease, and open the possibility that combining site chem. reactivity is a factor driving the expression of catalytic activity by autoantibodies.

L12 ANSWER 35 OF 57 CAPLUS COPYRIGHT 2003 ACS
1997:405951 Document No. 127:16498 Production of antibodies, and ***medical*** uses involving antibodies. Bradwell, Arthur Randell (Binding Site Limited, UK; Bradwell, Arthur Randell). PCT Int. Appl. WO 9717372 A1 19970515, 70 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1996-GB2638 19961030. PRIORITY: GB 1995-22554 19951103; GB 1996-15578 19960724.

AB A naive B-cell can be prevented from having a primary immunol. response to an antigen if antibodies to the antigen are already present. This can be exploited technol. by challenging an animal with unwanted antibodies, allowing it to produce desired antibodies that are more specific antibodies than has hitherto been possible. This enables better immunol. test kits to be produced. The feature of naive B-cell switch off can also be industrially applied to prevent an immunol. response to repeated administrations of physiol. active substances to a patient. The desire antibody is specific for antigen including streptokinase, TNF, selectin, cytokine, tumor targeting antibody, erythropoietin, Factor VIII, anti-botulism or diphtheria antiserum, antitoxin, or interferon.

L12 ANSWER 36 OF 57 CAPLUS COPYRIGHT 2003 ACS
1997:204244 Document No. 126:198560 Compositions and methods for catalyzing hydrolysis of HIV gp120. Paul, Sudhir; Kalaga, Ravishankar (University of Nebraska Board of Regents, USA; Paul, Sudhir; Kalaga, Ravishankar). PCT Int. Appl. WO 9703696 A1 19970206, 38 pp. DESIGNATED STATES: W: CA, CN, JP, US; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US12025 19960719. PRIORITY: US 1995-1321 19950721.

AB A catalytic antibody and components thereof which cleave HIV gp120 are disclosed. Methods of isolating, cloning and purifying such antibodies or antibody components from patients with AIDS and systemic lupus erythematosus are also described. The compns. described may provide utility in the treatment of HIV or HIV-1 infection.

L12 ANSWER 39 OF 57 CAPLUS COPYRIGHT 2003 ACS
1997:103412 Document No. 126:212008 ***Catalytic*** ***antibodies***: the rerouting of chemical reactions. Towards ***electrophilic*** aromatic substitution by carbon dioxide. Yli-Kauhaluoma, Jart T.; Janda, Kim D. (Chemical Process Technology, Technical Research Center of Finland, Espoo, FIN-02150, Finland). Annals of the New York Academy of Sciences, 799(Enzyme Engineering XIII), 26-31 (English) 1996. CODEN: ANYAA9. ISSN: 0077-8923. Publisher: New York Academy of Sciences.

GI

/ Structure 1 in file .gra /

AB Thiomethylation of 2-chloro-5-nitropyridine was accomplished in 2 steps (92% yield) employing sodium sulfide in DMF-water and alkylating subsequently with MeI. The sulfide was oxidized to the sulfone by potassium permanganate in aq. HOAc (87% yield). 2-Methylsulfonyl-5-nitropyridine was hydrogenated over Pd to give 99% of the corresponding aminopyridine, which was acylated with glutaric anhydride in the presence of N,N-diisopropylethylamine (91% yield). Oxidn. of the pyridine N by dimethyldioxirane in acetone at room temp. gave 76% hapten I, which was the pyridine N-oxide transition state analog of the Kolbe-Schmitt reaction. The activated hapten was used to immunize mice for the prodn. of monoclonal antibodies.

L12 ANSWER 40 OF 57 CAPLUS COPYRIGHT 2003 ACS
1997:13620 Document No. 126:114833 Proteolytic antibodies. Paul, Sudhir

(Dep. Anesthesiology, Pathology Microbiol. Internal Med., Eppley Cancer Res. Inst., Omaha, NE, 68198-6830, USA). Israel Journal of Chemistry, 36(2), 207-214 (English) 1996. CODEN: ISJCAT. ISSN: 0021-2148. Publisher: Laser Pages Publishing.

AB A review with 53 refs. Catalytic activities are known to arise naturally in antibodies. Several naturally-occurring peptides, synthetic protease substrates, DNA, and esters are known to be cleaved by antibodies. There is increased prodn. of antigen-specific ***catalytic*** ***antibodies*** in autoimmune ***disease*** . Polyreactive catalytic antibodies are present in unimmunized donors. Antibody light chains isolated from multiple myeloma patients frequently express proteolytic activity. Immunization protocols using as immunogens the ground state of a naturally-occurring polypeptide, anti-enzyme antibodies, or the enzyme itself are known to provoke catalytic antibody synthesis. Active site residues in the light chain subunit serve as the catalytic residues in a model antibody with peptide bond cleaving activity. A split-site model in which distinct amino acids serve as the essential catalytic residues and substrate ground-state recognition residues has been developed from mutagenesis studies. Engineering of the available antibodies could potentially generate improved catalysts. The possible mechanisms underlying proteolysis by natural antibodies and evolution of the catalytic activity are reviewed.

L12 ANSWER 41 OF 57 CAPLUS COPYRIGHT 2003 ACS

1997:13431 Document No. 126:115040 Structural studies of ***catalytic*** ***antibodies*** . Stevens, Raymond C.; Hsieh-Wilson, Linda C.; Santarsiero, Bernard D.; Wedemayer, Gary J.; Spiller, Ben; Wang, Leo H.; Barnes, Dwight; Ulrich, Helle D.; Patten, Phillip A.; Romesberg, Floyd E.; Schultz, Peter G. (Dep. Chem. Howard Hughes Med. Inst., Univ. California, Berkeley, CA, 94720, USA). Israel Journal of Chemistry, 36(2), 121-132 (English) 1996. CODEN: ISJCAT. ISSN: 0021-2148. Publisher: Laser Pages Publishing.

AB A panel of ***catalytic*** ***antibodies*** which catalyze ester hydrolysis, transesterification, porphyrin metalation, Diels-Alder, and redox reactions has been selected for crystallog. study. While these examples are only a handful of the ***catalytic*** ***antibodies*** generated to date, they represent distinct and important aspects of antibody catalysis. Since the first reports of catalysis, a great deal of progress has been made with respect to the scope, selectivity, and efficiency of ***antibody*** catalysis and strategies for generating ***catalytic*** ***antibodies*** . However, it is clear that further progress in the field will benefit greatly from a detailed understanding of the mol. interactions occurring in the combining site. High-resoln. crystallog. data should allow the importance of general base catalysis, entropy effects, ***electrophilic*** catalysis, and transition-state stabilization to be evaluated. Antibody and enzyme active sites have been shown to share considerable structural and mechanistic similarity, and ongoing structure-function studies of ***catalytic*** ***antibodies*** may enhance our understanding of the mechanisms and evolution of enzymic catalysis. Structural studies of antibodies which perform a biol. or highly selective reaction should enhance our ability to generate catalysts for important synthetic applications. Finally, the combination of high-resoln. crystallog. anal. with rational mutagenesis should provide a basis for engineering antibodies with enhanced properties.

L12 ANSWER 42 OF 57 CAPLUS COPYRIGHT 2003 ACS

1996:705058 Document No. 126:54519 The ***medical*** potential of ***catalytic*** ***antibodies*** . Blackburn, G. Michael; Datta, Anita; Patridge, Lynda J. (Krebs Inst., Sheffield Univ., Sheffield, S3 7HF, UK). Pure and Applied Chemistry, 68(11), 2009-2016 (English) 1996. CODEN: PACHAS. ISSN: 0033-4545. Publisher: Blackwell.

AB ***Catalytic*** ***antibodies*** are relatively slow catalysts with turnover nos. some 106 less than is common for enzymes. However, they have the advantage of high affinity for a pre-selected substrate and the ability to carry out a predetd. chem. transformation with an efficiency that is adequate for ***medical*** application. In a feasibility study, we have chosen to investigate antibody catalysis of carbamate ester cleavage and apply it to achieve cell-kill in a system that is a paradigm for ADAPT: Antibody Directed ***Abzyme*** Prodrug Therapy. We have differentiated the two alternative pathways for

hydrolysis of an aryl carbamate ester by the synthesis of a tetrahedral phosphonamidate ester transition state analog for the disfavored BAc2 pathway and its use as a hapten to generate antibody catalysts. Such ***abzymes*** can lower the activation energy of the BAC2 pathway relative to that for the normal ElcB hydrolysis. Of the antibodies thus elicited, DF8-D5 proved to be the best catalyst, showing good Michaelis-Menten kinetics and strong inhibition by the hapten. Hammett anal. with a range of substrates gave .rho. = +0.53 for the DF8-D5 hydrolysis and .rho. = 2.63 for the hydroxide mediated reaction of a range of p-substituted carbamates, which confirms the mechanistic switch. When a carbamate ester of a phenolic mustard is used as substrate, a cognate antibody EA11-D7 can cause cell kill of human colorectal carcinoma cells in tissue culture as a result of the same catalytic cleavage process to release a cytotoxic phenolic mustard.

L12 ANSWER 46 OF 57 CAPLUS COPYRIGHT 2003 ACS

1996:91668 Document No. 124:139292 ***Catalytic*** ***antibodies*** . What is done? What is learned from enzymes. Hiratake, Jun; Oda, Junichi (Inst. Chem. Res., Kyoto Univ., Uji, 611, Japan). Igaku no Ayumi, 175(11/12), 809-12 (Japanese) 1995. CODEN: IGAYAY. ISSN: 0039-2359. Publisher: Ishiyaku.

AB A review with 11 refs. Several examples of ***catalytic*** ***antibodies*** , comparison of their nature with that of enzymes, and their possible application in ***medical*** field were described.

L12 ANSWER 49 OF 57 CAPLUS COPYRIGHT 2003 ACS

1995:467335 Document No. 122:211709 Catalytic activity of anti-thyroglobulin antibodies. Li, Lan; Paul, Sudhir; Tyutyulkova, Sonia; Kazatchkine, Michel D.; Kaveri, Srinivas (Eppley Cancer Res. Inst., Univ. Nebraska Med. Center, Omaha, 68198, USA). Journal of Immunology, 154(7), 3328-32 (English) 1995. CODEN: JOIMA3. ISSN: 0022-1767. Publisher: American Association of Immunologists.

AB Thyroglobulin (Tg)-specific autoantibodies from a patient with Hashimoto's thyroiditis hydrolyzed radiolabeled Tg, shown by prodn. of several smaller sized products on SDS electrophoresis gels. The apparent Km value for Tg was in the nanomolar range, a property typical of an Ab combining site. The Tg antibodies also hydrolyzed tripeptide-methylcoumarinamide (MCA) substrates with lower affinity, displaying a preference for Arg-MCA and Lys-MCA contg. conjugates. The hydrolysis of one of these conjugates, Pro-Phe-Arg-MCA, was inhibited competitively by Tg, suggesting a catalytic site located in the Ab combining site. In control expts., 1) the hydrolytic activities were removed by immunoadsorption with immobilized anti-human IgG; 2) IgG depleted of the Tg-specific Abs by affinity chromatog. did not display Tg and Pro-Phe-Arg-MCA hydrolyzing activities; and 3) the peptide-MCA hydrolyzing activity tracked exactly with the 150-kDa IgG peak on a gel filtration column run in denaturing solvent (6 M guanidine chloride).